PATENT COOPERATION TREATY

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From the
INTERNATIONAL SEARCHING AUTHORITY

REC'D 06 JUN 2005
WIPO PCT

PCT

To:

see form PCT/ISA/220

28/1X

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Applicant's or agent's file reference see form PCT/ISA/220	Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet) **FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2005/000083	04.01.2005	06.01.2004

International Patent Classification (IPC) or both national classification and IPC
A61K31/13, A61K45/06, A61P25/18, A61P25/22, A61P25/24

Applicant
YALE UNIVERSITY

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-8

because:

☒ the said international application, or the said claims Nos. 1-8 (industrial applicability) relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form ☐ has not been furnished

☐ does not comply with the standard

the computer readable form ☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	8,13,16,22,23
	No:	Claims	1-7,9-12,14,15,17-21,24
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-24
Industrial applicability (IA)	Yes:	Claims	9-24
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 1-8 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The following documents (D1-D4) are referred to in this written opinion; the numbering results from the order of citations found in the Search Report (SR) and will be adhered to in the rest of the procedure. The cited passage(s) for each citation will be considered unless otherwise specified.

V.1. Novelty

V.1.1. Claims 1-7, 9-12, 14, 15, 17-21, 24 do not appear to be novel in the sense of Article 33 (2) PCT, the reasons being as follows:

a) D2 discloses pharmaceutical formulations for treating tobacco, nicotine, cocaine and alcohol addiction, comprising a nicotinic acetylcholine receptor antagonist and an antidepressant such as tricyclic antidepressants, norepinephrine dopamine reuptake inhibitors, selective serotonin reuptake inhibitors, selective norepinephrine reuptake inhibitors and monoamine oxidase inhibitors. In particular, oral compositions comprising mecamylamine hydrochloride and bupropion or doxepin are mentioned, which may be formulated to release the active agents over an extended period of time.

Thus, D2 anticipates the subject-matter of claims 9-12, 14, 15, 17-21, 24.

In this context it is reminded that a new therapeutic indication (i.e. treatment of mood disorders) can only restore the novelty of a known product/composition, if this

product/composition has not yet been used for therapeutic purposes in the state of the art.

In the present case however, the claimed composition has already been employed in therapy.

b) D3 describes the combined use of mecamylamine and sertraline for the treatment of depression and mood swings, and hence takes away the novelty of claims 1-7.

V.1.2. Claims 8, 13, 16, 22, 23 appear to be novel over the available prior art.

V.2. Inventive step

V.2.1. Being not new, the subject-matter of present claims 1-7, 9-12, 14, 15, 17-21, 24 cannot be considered as inventive either.

V.2.2. Claims 8, 13, 16, 22, 23:

a) D3, which is considered to represent the most relevant state of the art, discloses the combined use of mecamylamine and sertraline for the treatment of depression and mood swings.

b) The subject-matter of claims 8, 13, 16, 22, 23 differs from D3 in that the in D3 described active substances are not formulated as a single pharmaceutical formulation.

c) Nevertheless, oral pharmaceutical formulations comprising a nicotinic acetylcholine receptor antagonist and a selective serotonin reuptake inhibitor (fluoxetine, fluvoxamine, paroxetine, sertraline, trazodone) are well-known in prior art (see D2). Hence, it would be obvious to the person skilled in the art to combine the teachings of D3 with D2, and so to arrive at the claimed invention.

Therefore, claims 8, 13, 16, 22, 23 do not appear to involve an inventive step in the sense of Article 33(3) PCT.

V.3. Industrial Applicability

For the assessment of the present claims 1-8 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.